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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/091,240	03/05/2002	Matthew Shair	2001180-0051 (HU 11588-98	7192

24280 7590 09/13/2004

Choate, Hall & Stewart
Exchange Place
53 State Street
Boston, MA 02109

EXAMINER	
TRAN, MY CHAU T	

ART UNIT	PAPER NUMBER
1639	

DATE MAILED: 09/13/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/091,240	SHAIR ET AL.	
	Examiner	Art Unit	
	MY-CHAU T TRAN	1639	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *07 June 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-47* is/are pending in the application.

4a) Of the above claim(s) *1,8,11-17,21-25,27-29 and 34-47* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *2-7,9,10,18-20,26 and 30-33* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *05 March 2002* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *6/26/03*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Status of Claims

1. Applicant's response filed 6/24/2003 and 6/7/2004 is acknowledged and entered.

2. Claims 1-47 are pending.

Election/Restrictions

3. Applicant's election of Group II (Claims 2-33) in the reply filed on 6/24/2003 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

4. Claims 1, and 34-47 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to ***nonelected inventions***, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on 6/24/2003.

5. Applicant has elected the following species for the elected invention (Claims 2-33) in the reply filed on 6/24/2003 and 6/7/2004:

a. A species of test compound. Applicant elected small molecule, which is Taxol.

b. A species of molecular sensor. Applicant elected 2,3-diaminonaphthalene (DAN), which is attached to the solid support via an amide bond shown in figure 4.

c. A species of decoding tag. Applicant elected inert halogenated compound.

d. A species of inducible reporter gene. Applicant elected nitric oxide synthase.

e. A species of reporter gene product. Applicant elected nitric oxide.

f. A species of chemical compound. Applicant elected nitric oxide.

g. A species of cell. Applicant elected yeast.

h. A species of solid support. Applicant elected solid phase resin beads (e.g., aminomethyl-TENTAGEL resin).

6. Claims 8, 11-17, 21-25, and 27-29 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to ***nonelected species***, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on 6/24/2003 and 6/7/2004.

Priority

7. This application claims priority to a provisional application 60/273,736 filed 3/5/2001.

Information Disclosure Statement

8. The information disclosure statements (IDS) filed on 6/26/2003 are acknowledged and considered as noted on PTO-1449.

Drawings

9. The drawings were received on 3/5/2002. These drawings are acceptable.

Specification

10. The disclosure is objected to because it contains an embedded hyperlink and/or other form of browser-executable code (see specification e.g. pg. 4, line 16). Applicant is required to delete the embedded hyperlink and/or other form of browser-executable code that can be found through out the specification. See MPEP § 608.01.

11. Claims 2-7, 9-10, 18-20, 26, and 30-33 are treated on the merit in this Office Action.

Claim Rejections - 35 USC § 112

12. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

13. Claims 2-7, 9-10, 18-20, 26, and 30-33 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claims contains subject matter, which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a written description rejection.

The instant claim 2 recites a method of identifying a test compound that affects a biological event of interest. The method comprises the steps of: 1) providing a plurality of test compounds; 2) providing cells containing an inducible reporter gene, wherein expression of the reporter gene results in the production of a reporter gene product; 3) contacting the cells with the plurality of test compounds; and 4) identifying test compounds which promote or inhibit a

biological event based on production of the reporter gene product. The reporter gene product is secreted by the cell, detectable, and its the presence indicates occurrence or non-occurrence of a selected biological event.

The specification disclosure does not sufficiently teach the claimed method of identifying a test compound that affects a biological event of interest wherein the biological event of interest is being detected using ***any*** type of inducible reporter gene that produced a product, which is secreted by the cell and is detectable. The claimed method encompasses a broad genus of reporter genes that is use to detect biological event of interest, e.g. β-lactamase, luciferase, secreted alkaline phosphatase or green fluorescent protein. The specification description is directed to a screening method for detecting compound that affect protein binding event using nitric oxide synthase wherein the nitric oxide, i.e. reporter gene product, is secreted by the cell and is detected by nitric oxide sensor (see specification e.g. pg. 16, line 19 to pg. 17, line 4; pg. 18, line 8 to pg. 20, line 2; pg. 21, line 11 to pg. 23, line 15; fig. 2-6). The specification examples 2-8 are drawn to screening methods for detecting compound that affect protein binding event using nitric oxide synthase wherein the nitric oxide, i.e. reporter gene product, secreted by the cell is detected by nitric oxide sensor (see specification pages 27-36). This method clearly does not provide an adequate representation regarding a screening method that identifying test compound that affects a biological event of interest using ***any*** type of inducible reporter gene that produced a product, which is secreted by the cell and is detectable. Thus the specification does not teach the claimed method of identifying a test compound that affects a biological event of interest wherein the biological event of interest is being detected using ***any*** type of inducible reporter gene that produced a product, which is secreted by the cell and is detectable.

Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, makes clear that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention.* The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed.*" (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See Vas-Cath at page 1116.).

With the exception of screening method for detecting compound(s) that affect the protein binding event using nitric oxide synthase wherein the nitric oxide, i.e. reporter gene product, secreted by the cell is detected by nitric oxide sensor disclosed by the specification, the skilled artisan cannot envision the method of identifying a test compound that affects a biological event of interest wherein the biological event of interest is being detected using ***any*** type of inducible reporter gene that produced a product, which is secreted by the cell and is detectable. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it. See Fiers v. Revel, 25 USPQ2d 1601, 1606 (CAFC 1993) and Amgen Inc. V. Chugai Pharmaceutical Co. Ltd., 18 USPQ2d 1016. In Fiddes v. Baird, 30 USPQ2d 1481, 1483, claims directed to mammalian FGF's were found unpatentable due to lack of written description for the broad class. The specification provided only the bovine sequence.

Finally, University of California v. Eli Lilly and Co., 43 USPQ2d 1398, 1404, 1405 held that:

...To fulfill the written description requirement, a patent specification must describe an invention and do so in sufficient detail that one skilled in the art can clearly conclude that "the inventor invented the claimed invention." *Lockwood v. American Airlines, Inc.*, 107 F.3d 1565, 1572, 41 USPQ2d 1961, 1966 (1997); In *re Gosteli*, 872 F.2d 1008, 1012, 10 USPQ2d 1614,

1618 (Fed. Cir. 1989) (" [T]he description must clearly allow persons of ordinary skill in the art to recognize that [the inventor] invented what is claimed."). Thus, an applicant complies with the written description requirement "by describing the invention, with all its claimed limitations, not that which makes it obvious," and by using "such descriptive means as words, structures, figures, diagrams, formulas, etc., that set forth the claimed invention." *Lockwood*, 107 F.3d at 1572, 41 USPQ2d at 1966.

In the present instance, the specification does not teach claimed method identifying a test compound that affects a biological event of interest wherein the biological event of interest is being detected using ***any*** type of inducible reporter gene that produced a product, which is secreted by the cell and is detectable. Therefore, only the screening method for detecting protein binding event using nitric oxide synthase wherein the nitric oxide, i.e. reporter gene product, secreted by the cell is detected by nitric oxide sensor, but not the full breadth of the claim method meet the written description provision of 35 U.S.C 112, first paragraph.

14. Claims 2-3, and 5 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claims contains subject matter, which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a written description rejection.

The instant claim 2 recites a method of identifying a test compound that affects a biological event of interest. The method comprises the steps of: 1) providing a plurality of test compounds; 2) providing cells containing an inducible reporter gene, wherein expression of the reporter gene results in the production of a reporter gene product; 3) contacting the cells with the plurality of test compounds; and 4) identifying test compounds which promote or inhibit a biological event based on production of the reporter gene product. The reporter gene product is

secreted by the cell, detectable, and its the presence indicates occurrence or non-occurrence of a selected biological event. Claim 3 claimed that the plurality of test compounds is attached to a solid support through a cleavable linkage. Claim 5 claimed that the solid support is associated with a molecular sensor.

The specification disclosure does not sufficiently teach the claimed method of identifying a test compound that affects a biological event of interest wherein ***any*** type of molecular sensor is use to detect the reporter gene product wherein the production of the reporter gene product identifying the test compound(s) that affect a biological event. The claimed method encompasses a broad genus of molecular sensor that is use to detect the reporter gene product in order to identify test compound(s) that affect a biological event, e.g. fluorescent label, dendrimer, or green fluorescent protein. The specification description is directed to the use of nitric oxide sensor to detect nitric oxide produce by nitric oxide synthase in the screening method for detecting compound(s) that affected protein binding event (see specification e.g. pg. 16, line 19 to pg. 17, line 4; pg. 18, line 8 to pg. 20, line 2; pg. 21, line 11 to pg. 23, line 15; fig. 2-6). The specification examples 2-8 are drawn to the use of nitric oxide sensor to detect nitric oxide produce by nitric oxide synthase in the screening method for detecting compound(s) that affected protein binding event (see specification pages 27-36). This method clearly does not provide an adequate representation regarding the claimed method of identifying a test compound that affects a biological event of interest wherein ***any*** type of molecular sensor is use to detect the reporter gene product wherein the production of the reporter gene product identifying the test compound(s) that affect a biological event. Thus the specification does not teach the claimed method of identifying a test compound that affects a biological event of interest wherein ***any***

type of molecular sensor is use to detect the reporter gene product wherein the production of the reporter gene product identifying the test compound(s) that affect a biological event.

Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, makes clear that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention.* The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed.*" (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See Vas-Cath at page 1116.).

With the exception of the use of nitric oxide sensor to detect nitric oxide produce by nitric oxide synthase in the screening method for detecting compound(s) that affected protein binding event disclosed by the specification, the skilled artisan cannot envision the method of identifying a test compound that affects a biological event of interest wherein ***any*** type of molecular sensor is use to detect the reporter gene product wherein the production of the reporter gene product identifying the test compound(s) that affect a biological event. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it. See Fiers v. Revel, 25 USPQ2d 1601, 1606 (CAFC 1993) and Amgen Inc. V. Chugai Pharmaceutical Co. Ltd., 18 USPQ2d 1016. In Fiddes v. Baird, 30 USPQ2d 1481, 1483, claims directed to mammalian FGF's were found unpatentable due to lack of written description for the broad class. The specification provided only the bovine sequence.

Finally, University of California v. Eli Lilly and Co., 43 USPQ2d 1398, 1404, 1405 held that:

...To fulfill the written description requirement, a patent specification must describe an invention and do so in sufficient detail that one skilled in the art can clearly conclude that "the

inventor invented the claimed invention." *Lockwood v. American Airlines, Inc.*, 107 F.3d 1565, 1572, 41 USPQ2d 1961, 1966 (1997); In *re Gosteli*, 872 F.2d 1008, 1012, 10 USPQ2d 1614, 1618 (Fed. Cir. 1989) (" [T]he description must clearly allow persons of ordinary skill in the art to recognize that [the inventor] invented what is claimed."). Thus, an applicant complies with the written description requirement "by describing the invention, with all its claimed limitations, not that which makes it obvious," and by using "such descriptive means as words, structures, figures, diagrams, formulas, etc., that set forth the claimed invention." *Lockwood*, 107 F.3d at 1572, 41 USPQ2d at 1966.

Additionally, Cf. University of Rochester v G.D. Searle & Co., Inc., Monsanto Company, Pharmacia Corporation, and Pfizer Inc., No. 03-1304, 2004 WL 260813 (Fed. Cir., Feb. 13, 2004) held that:

Regardless whether a compound is claimed per se or a method is claimed that entails the use of the compound, the inventor cannot lay claim to that subject matter unless he can provide a description of the compound sufficient to distinguish infringing compounds from non-infringing compounds, or infringing methods from non-infringing methods.

In the present instance, the specification does not teach claimed method identifying a test compound that affects a biological event of interest wherein ***any*** type of molecular sensor is use to detect the reporter gene product wherein the production of the reporter gene product identifying the test compound(s) that affect a biological event. Therefore, only the method of using a nitric oxide sensor to detect nitric oxide produce by nitric oxide synthase in the screening method for detecting compound(s) that affected protein binding event, but not the full breadth of the claim method meet the written description provision of 35 U.S.C 112, first paragraph.

15. Claims 2-3, and 32 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claims contains subject matter, which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant

art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a written description rejection.

The instant claim 2 recites a method of identifying a test compound that affects a biological event of interest. The method comprises the steps of: 1) providing a plurality of test compounds; 2) providing cells containing an inducible reporter gene, wherein expression of the reporter gene results in the production of a reporter gene product; 3) contacting the cells with the plurality of test compounds; and 4) identifying test compounds which promote or inhibit a biological event based on production of the reporter gene product. The reporter gene product is secreted by the cell, detectable, and its the presence indicates occurrence or non-occurrence of a selected biological event. Claim 3 claimed that the plurality of test compounds is attached to a solid support through a cleavable linkage. Claim 33 claimed that the identifying step comprises sorting the solid supports using fluorescence-activated bead sorting (FABS).

The specification disclosure does not sufficiently teach the claimed method of identifying a test compound that affects a biological event of interest wherein the step of identifying the test compounds, which affect a biological event based on production of the reporter gene product, is a combination of detecting the production of the reporter gene product and sorting the solid supports using fluorescence-activated bead sorting wherein the bead has ***no*** fluorescence feature. The specification description is directed to the use of nitric oxide sensor to detect nitric oxide produce by nitric oxide synthase in the screening method for detecting compound(s) that affected protein binding event (see specification e.g. pg. 16, line 19 to pg. 17, line 4; pg. 18, line 8 to pg. 20, line 2; pg. 21, line 11 to pg. 23, line 15; fig. 2-6). The specification is silent of the detecting step wherein the test compound identification is base on both the detection of the reporter gene

product and sorting the solid supports using fluorescence-activated bead sorting wherein the bead has ***no*** fluorescence feature. The specification example 1 and fig. 2 are drawn to the use of nitric oxide sensor that is attached to the bead to detect nitric oxide produce by nitric oxide synthase in the screening method for detecting compound(s) that affected protein binding event (see specification pages 25-27). The method comprises the step of contacting cells with beads containing both the compound and the NO sensor; the compound is release from the bead by photolysis and react with the cell by entering the cell and affecting some intercellular process in the manner that results in expression of the inducible NO synthase reporter gene causing the production of NO; the NO sensor on the bead detect the NO by converting the bead to a fluorescent bead; the bead is identify by using fluorescence-activated bead sorting. This method clearly does not provide an adequate representation regarding the claimed method of identifying a test compound that affects a biological event of interest wherein the step of identifying the test compounds, which affect a biological event based on production of the reporter gene product, is a combination of detecting the production of the reporter gene product and sorting the solid supports using fluorescence-activated bead sorting wherein the bead has ***no*** fluorescence feature. Thus the specification does not teach the claimed method of identifying a test compound that affects a biological event of interest wherein the step of identifying the test compounds, which affect a biological event based on production of the reporter gene product, is a combination of detecting the production of the reporter gene product and sorting the solid supports using fluorescence-activated bead sorting wherein the bead ***no*** fluorescence feature.

Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, makes clear that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was

in possession *of the invention.* The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed.*" (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See Vas-Cath at page 1116.).

With the exception of using a nitric oxide sensor that is attached to the bead to detect nitric oxide produce by nitric oxide synthase in the screening method for detecting compound(s) that affected protein binding event disclosed by the specification, the skilled artisan cannot envision the method of identifying a test compound that affects a biological event of interest wherein the step of identifying the test compounds, which affect a biological event based on production of the reporter gene product, is a combination of detecting the production of the reporter gene product and sorting the solid supports using fluorescence-activated bead sorting wherein the bead has ***no*** fluorescence feature. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it. See Fiers v. Revel, 25 USPQ2d 1601, 1606 (CAFC 1993) and Amgen Inc. V. Chugai Pharmaceutical Co. Ltd., 18 USPQ2d 1016. In Fiddes v. Baird, 30 USPQ2d 1481, 1483, claims directed to mammalian FGF's were found unpatentable due to lack of written description for the broad class. The specification provided only the bovine sequence.

Finally, University of California v. Eli Lilly and Co., 43 USPQ2d 1398, 1404, 1405 held that:

...To fulfill the written description requirement, a patent specification must describe an invention and do so in sufficient detail that one skilled in the art can clearly conclude that "the inventor invented the claimed invention." *Lockwood v. American Airlines, Inc.*, 107 F.3d 1565, 1572, 41 USPQ2d 1961, 1966 (1997); In *re Gosteli*, 872 F.2d 1008, 1012, 10 USPQ2d 1614, 1618 (Fed. Cir. 1989) (" [T]he description must clearly allow persons of ordinary skill in the art to recognize that [the inventor] invented what is claimed."). Thus, an applicant complies with

the written description requirement "by describing the invention, with all its claimed limitations, not that which makes it obvious," and by using "such descriptive means as words, structures, figures, diagrams, formulas, etc., that set forth the claimed invention." *Lockwood*, 107 F.3d at 1572, 41 USPQ2d at 1966.

In the present instance, the specification does not teach the claimed method of identifying a test compound that affects a biological event of interest wherein the step of identifying the test compounds, which affect a biological event based on production of the reporter gene product, is a combination of detecting the production of the reporter gene product and sorting the solid supports using fluorescence-activated bead sorting wherein the bead has ***no*** fluorescence feature. Therefore, only the method of using a nitric oxide sensor that is attached to the bead to detect nitric oxide produce by nitric oxide synthase in the screening method for detecting compound(s) that affected protein binding event, but not the full breadth of the claim method meet the written description provision of 35 U.S.C 112, first paragraph.

16. Claims 2-3, and 33 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claims contains subject matter, which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a written description rejection.

The instant claim 2 recites a method of identifying a test compound that affects a biological event of interest. The method comprises the steps of: 1) providing a plurality of test compounds; 2) providing cells containing an inducible reporter gene, wherein expression of the reporter gene results in the production of a reporter gene product; 3) contacting the cells with the plurality of test compounds; and 4) identifying test compounds which promote or inhibit a

biological event based on production of the reporter gene product. The reporter gene product is secreted by the cell, detectable, and its the presence indicates occurrence or non-occurrence of a selected biological event. Claim 3 claimed that the plurality of test compounds is attached to a solid support through a cleavable linkage. Claim 33 claimed that the identifying step comprises decoding tags on the solid support which correspond to the synthetic history of the test compound attached or was once attached to the bead or structural features of the test compound. It is interpreted that the identifying step is a combination of detecting the production of the reporter gene product and decoding the decoding tag on the solid support.

The specification disclosure does not sufficiently teach the claimed method of identifying a test compound that affects a biological event of interest wherein the step of identifying the test compounds, which affect a biological event based on production of the reporter gene product, is a combination of detecting the production of the reporter gene product and decoding the decoding tag on the solid support. The specification description is directed to the use of nitric oxide sensor to detect nitric oxide produce by nitric oxide synthase in the screening method for detecting compound(s) that affected protein binding event (see specification e.g. pg. 16, line 19 to pg. 17, line 4; pg. 18, line 8 to pg. 20, line 2; pg. 21, line 11 to pg. 23, line 15; fig. 2-6). The specification is silent of the detecting step wherein the test compound identification is base on both the detection of the reporter gene product and decoding the decoding tag on the solid support. The specification examples 2-8 are drawn to the use of nitric oxide sensor to detect nitric oxide produce by nitric oxide synthase in the screening method for detecting compound(s) that affected protein binding event (see specification pages 27-36). This method clearly does not provide an adequate representation regarding the claimed method of identifying a test compound

that affects a biological event of interest wherein the step of identifying the test compounds, which affect a biological event based on production of the reporter gene product, is a combination of detecting the production of the reporter gene product and decoding the decoding tag on the solid support. Thus the specification does not teach the claimed method of identifying a test compound that affects a biological event of interest wherein the step of identifying the test compounds, which affect a biological event based on production of the reporter gene product, is a combination of detecting the production of the reporter gene product and decoding the decoding tag on the solid support.

Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, makes clear that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention.* The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed.*" (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See Vas-Cath at page 1116.).

With the exception of using a nitric oxide sensor to detect nitric oxide produce by nitric oxide synthase in the screening method for detecting compound(s) that affected protein binding event disclosed by the specification, the skilled artisan cannot envision the method of identifying a test compound that affects a biological event of interest wherein the step of identifying the test compounds, which affect a biological event based on production of the reporter gene product, is a combination of detecting the production of the reporter gene product and decoding the decoding tag on the solid support. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it. See

Fiers v. Revel, 25 USPQ2d 1601, 1606 (CAFC 1993) and Amgen Inc. V. Chugai Pharmaceutical Co. Ltd., 18 USPQ2d 1016. In Fiddes v. Baird, 30 USPQ2d 1481, 1483, claims directed to mammalian FGF's were found unpatentable due to lack of written description for the broad class. The specification provided only the bovine sequence.

Finally, University of California v. Eli Lilly and Co., 43 USPQ2d 1398, 1404, 1405 held that:

...To fulfill the written description requirement, a patent specification must describe an invention and do so in sufficient detail that one skilled in the art can clearly conclude that "the inventor invented the claimed invention." *Lockwood v. American Airlines, Inc.*, 107 F.3d 1565, 1572, 41 USPQ2d 1961, 1966 (1997); In *re Gosteli*, 872 F.2d 1008, 1012, 10 USPQ2d 1614, 1618 (Fed. Cir. 1989) (" [T]he description must clearly allow persons of ordinary skill in the art to recognize that [the inventor] invented what is claimed."). Thus, an applicant complies with the written description requirement "by describing the invention, with all its claimed limitations, not that which makes it obvious," and by using "such descriptive means as words, structures, figures, diagrams, formulas, etc., that set forth the claimed invention." *Lockwood*, 107 F.3d at 1572, 41 USPQ2d at 1966.

In the present instance, the specification does not teach the claimed method of identifying a test compound that affects a biological event of interest wherein the step of identifying the test compounds, which affect a biological event based on production of the reporter gene product, is a combination of detecting the production of the reporter gene product and decoding the decoding tag on the solid support. Therefore, only the method of using a nitric oxide sensor to detect nitric oxide produce by nitric oxide synthase in the screening method for detecting compound(s) that affected protein binding event, but not the full breadth of the claim method meet the written description provision of 35 U.S.C 112, first paragraph.

17. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

18. Claims 2-7, 9-10, 18-20, 26, and 30-33 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

a) The contacting step of Claim 2 and the claimed structural feature of the test compounds of Claim 3 are incomplete and indefinite. Claim 2 recites the step of "*contacting the cells with the plurality of test compounds*". Claim 3 recites that the test compounds are attached to a solid support through a cleavable linkage. The limitations combination of Claims 2 and 3 are incomplete and indefinite because it is unclear how the compounds can contact with the cell when they are attached to a solid support, i.e. there is no correlation of how the test compounds that are on a single solid support be in contact with the cells in order to affect a biological event that is based on the production of the reporter gene product. Thus limitations combination of Claims 2 and 3 are incomplete and indefinite.

b) The identifying step of Claim 2, the claimed structural feature of the test compounds of Claim 3 and the identifying step of Claim 32 are incomplete and indefinite. Claim 2 recites the step of "*identifying test compounds which promote or inhibit a biological event based on production of the reporter gene product*", which is interpreted as detecting the reporter gene product to identify the test compounds. Claim 3 recites that the test compounds are attached to a solid support through a cleavable linkage. Claim 32 recite the identifying step of "*sorting the solid supports using fluorescence-activated bead sorting (FABS)*". The limitations combination of Claims 2, 3, and 32 are incomplete and indefinite because there is ***no*** fluorescence feature on the solid support and the identifying step of Claim 32 contradict the identifying step of Claim 2, i.e. Claim 2 detect the reporter gene product ***not*** the solid support. Thus limitations combination

of Claims 2, 3, and 32 are incomplete and indefinite. It is suggested that applicant amend claim 32 by changing "comprises" to "further comprises".

c) The identifying step of Claim 2, the claimed structural feature of the test compounds of Claim 3 and the identifying step of Claim 33 are incomplete and indefinite. Claim 2 recites the step of "*identifying test compounds which promote or inhibit a biological event based on production of the reporter gene product*", which is interpreted as detecting the reporter gene product to identify the test compounds. Claim 3 recites that the test compounds are attached to a solid support through a cleavable linkage. Claim 32 recite the identifying step of "*decoding tags on the solid support which correspond to the synthetic history of the test compound attached or was once attached to the bead or structural features of the test compound*". The limitations combination of Claims 2, 3, and 32 are incomplete and indefinite because the is ***no*** fluorescence feature is on the solid support and the identifying step of Claim 33 contradict the identifying step of Claim 2, i.e. Claim 2 detect the reporter gene product ***not*** the decoding tag on the solid support. Thus limitations combination of Claims 2, 3, and 33 are incomplete and indefinite.

d) Claim 9 recites the limitation "molecular sensor" in line 1. There is insufficient antecedent basis for this limitation in the claim 4.

Claim Rejections - 35 USC § 102

19. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

20. Claims 2, 10, 18-20, 26, and 30-31 are rejected under 35 U.S.C. 102(b) as being anticipated by Foulkes et al. (US Patent 5,580,722).

The instant claim 2 recites a method of identifying a test compound that affects a biological event of interest. The method comprises the steps of: 1) providing a plurality of test compounds; 2) providing cells containing an inducible reporter gene, wherein expression of the reporter gene results in the production of a reporter gene product; 3) contacting the cells with the plurality of test compounds; and 4) identifying test compounds which promote or inhibit a biological event based on production of the reporter gene product. The reporter gene product is secreted by the cell, detectable, and its the presence indicates occurrence or non-occurrence of a selected biological event.

Foulkes et al. teach the method of determining whether a chemical not previously known to be a modulator of protein biosynthesis is capable of specifically transcriptionally modulating the expression of a gene encoding a protein of interest (see e.g. Abstract; col. 11, lines 12-29; col. 11, line 60 to col. 12, line 20; col. 18, line 43 to col. 19, line 3; col. 93, Claim 1). The method comprises the step of: (a) contacting a sample which contains a predefined number of identical eukaryotic cells (refers to the step of providing cells and claim 26) with a predetermined concentration of the chemical to be tested (refers to the step of providing a plurality of test compounds and claim 10), each such cell comprising a single DNA construct consisting essentially of in 5' to 3' order (i) a modulatable transcriptional regulatory sequence of the gene encoding the protein of interest, (ii) a promoter of the gene encoding the protein of interest, and (iii) a reporter gene which expresses a polypeptide (refers to reporter gene product) capable of producing a detectable signal, coupled to, and under the control of, the promoter, under conditions such that the chemical if capable of acting as a transcriptional modulator of the gene encoding the protein of interest, causes a measurable detectable signal to be produced by

the polypeptide expressed by the reporter gene (step (a) refers to the claimed contacting step and claim 18); (b) quantitatively determining the amount of the signal so produced; and (c) comparing the amount so determined with the amount of produced signal detected in the absence of any chemical being tested and upon contacting the sample with other chemicals so as to thereby identify the chemical as a chemical which causes a change in the detectable signal produced by the polypeptide, and determining whether the chemical specifically transcriptionally modulates expression of the gene associated with the treatment of one or more symptoms of the cardiovascular disease (step (c) refers to the claimed identifying step) (see e.g. col. 11, lines 12-29; col. 11, line 60 to col. 12, line 20; col. 18, line 43 to col. 19, line 3; col. 93, Claim 1). The protein of interest includes nitric oxide synthase (refers to claims 19-20, and 30-31) (see e.g. col. 22, lines 1-21). Thus the method of Foulkes et al. anticipates the presently claimed method.

21. Claims 2-4, 10, 18, and 26 are rejected under 35 U.S.C. 102(b) as being anticipated by Borchardt et al. (*Chemistry & Biology*, **1997**, 4(12):961-968).

The instant claim 2 recites a method of identifying a test compound that affects a biological event of interest. The method comprises the steps of: 1) providing a plurality of test compounds; 2) providing cells containing an inducible reporter gene, wherein expression of the reporter gene results in the production of a reporter gene product; 3) contacting the cells with the plurality of test compounds; and 4) identifying test compounds which promote or inhibit a biological event based on production of the reporter gene product. The reporter gene product is secreted by the cell, detectable, and its the presence indicates occurrence or non-occurrence of a selected biological event.

Borchardt et al. teach methods of detecting small molecule-protein interaction within yeast cells (see e.g. Abstract; pg. 962, right col., lines 1-12; pg. 963, right col., line 41 to pg. 964,

right col. 25; pg. 965, left col., line 15 to pg. 966, right col., line 8). The methods comprise the steps of contacting the small molecules with the yeasts cell (refers to claim 26), and detecting the small molecule-protein binding via of cell growth or lack of cell growth (see e.g. pg. 963, right col., line 41 to pg. 964, right col. 25; pg. 965, left col., line 15 to pg. 966, right col., line 8). In the growth inhibition assay the binding of rapamycin to its protein targets (refers to reporter gene) results in yeast cell arrest (refers to reporter gene product) and as a result inhibition of growth (see e.g. pg. 963, right col., line 41 to pg. 964, right col. 25; fig. 3). The small molecules are attached to resin via a photocleavable linker wherein the small molecules are release by irradiation with ultraviolet light (refers to claims 3-4, and 10) (see e.g. pg. 963, right col., lines 8-21; fig. 2). Borchardt et al. discloses that other type of readout can be use such as secretion of reporter enzymes or translocation of fluorescent proteins (see e.g. pg. 967, right col., lines 34-40). Thus the method of Borchardt et al. anticipates the presently claimed method.

22. Claims 2-4, 10, 18, and 33 are rejected under 35 U.S.C. 102(b) as being anticipated by Still et al. (US Patent 5,565,324).

The instant claim 2 recites a method of identifying a test compound that affects a biological event of interest. The method comprises the steps of: 1) providing a plurality of test compounds; 2) providing cells containing an inducible reporter gene, wherein expression of the reporter gene results in the production of a reporter gene product; 3) contacting the cells with the plurality of test compounds; and 4) identifying test compounds which promote or inhibit a biological event based on production of the reporter gene product. The reporter gene product is secreted by the cell, detectable, and its the presence indicates occurrence or non-occurrence of a selected biological event.

Still et al. teach methods and composition for encoding combinatorial chemistry (see e.g. Abstract; col. 3, lines 6-45). The methods includes the combinatorial synthesis that employs definable beads upon, which reactions are performed and to which the identifiers are bound, the method of screening the beads carrying the final product compounds for a characteristic of interest, and the method of analyzing the identifier tags attached to the solid supports for the reaction history of the final product compounds (see e.g. col. 3, lines 39-45; col. 5, lines 34-64; col. 29, line 65 to col. 30, line 51; col. 32, lines 14-22). The screening method comprises the steps of: 1) providing a plurality beads carrying the final product compounds (refers to claim 10 and step 1) (see e.g. col. 30, lines 1-6); 2) providing cells wherein binding a surface membrane protein (refers to reporter gene) produces an observable product (refers to reporter gene product) that is expressed (refers to claim 18 and step 2) (see e.g. col. 30, lines 32-42); 3) the final product compounds is detach from the bead in order to react with the cells (refers to step 3) (see e.g. col. 30, lines 13-15); 4) identifying the final product compounds that cause the expression of the observable product (refers to step 4) (see e.g. col. 30, lines 42-44; col. 32, lines 14-22). The final product compounds is attached to the bead via a cleavable linker that can be cleave by irradiation with light (refers to claims 3-4) (see e.g. col. 13, lines 44-64). Furthermore, the identifier tag attached to the solid supports is analyzed for the reaction history of the final product compounds (refers to claim 33) (see e.g. col. 6, lines 18-55; col. 26, lines 57-62; col. 32, lines 14-22). Thus the method of Still et al. anticipates the presently claimed method.

Claim Rejections - 35 USC § 103

23. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

24. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

25. Claims 2-4, 10, 18, 26, and 33 are rejected under 35 U.S.C. 103(a) as being unpatentable over Still et al. (US Patent 5,565,324) and Ashby et al. (US Patent 5,569,588).

The instant claim 2 recites a method of identifying a test compound that affects a biological event of interest. The method comprises the steps of: 1) providing a plurality of test compounds; 2) providing cells containing an inducible reporter gene, wherein expression of the reporter gene results in the production of a reporter gene product; 3) contacting the cells with the plurality of test compounds; and 4) identifying test compounds which promote or inhibit a biological event based on production of the reporter gene product. The reporter gene product is secreted by the cell, detectable, and its the presence indicates occurrence or non-occurrence of a selected biological event.

Still et al. teach methods and composition for encoding combinatorial chemistry (see e.g. Abstract; col. 3, lines 6-45). The methods includes the combinatorial synthesis that employs

definable beads upon, which reactions are performed and to which the identifiers are bound, the method of screening the beads carrying the final product compounds for a characteristic of interest such as physiological or biological activity, and the method of analyzing the identifier tags attached to the solid supports for the reaction history of the final product compounds (see e.g. col. 3, lines 39-45; col. 5, lines 34-64; col. 29, line 65 to col. 30, line 51; col. 32, lines 14-22). The screening method comprises the steps of: 1) providing a plurality beads carrying the final product compounds (refers to claim 10 and step 1) (see e.g. col. 30, lines 1-6); 2) providing cells wherein binding a surface membrane protein (refers to reporter gene) produces an observable product (refers to reporter gene product) that is expressed (refers to claim 18 and step 2) (see e.g. col. 30, lines 32-42); 3) the final product compounds is detach from the bead in order to react with the cells (refers to step 3) (see e.g. col. 30, lines 13-15); 4) identifying the final product compounds that cause the expression of the observable product (refers to step 4) (see e.g. col. 30, lines 42-44; col. 32, lines 14-22). The final product compounds is attached to the bead via a cleavable linker that can be cleave by irradiation with light (refers to claims 3-4) (see e.g. col. 13, lines 44-64). Furthermore, the identifier tag attached to the solid supports is analyzed for the reaction history of the final product compounds (refers to claim 33) (see e.g. col. 6, lines 18-55; col. 26, lines 57-62; col. 32, lines 14-22).

The method of Still et al. does not expressly include using yeast cell in the method of screening compounds for a characteristic of interest such as physiological or biological activity.

Ashby et al. teach the methods and compositions for modeling the transcriptional responsiveness of an organism to a candidate drug (see e.g. Abstract; col. 1, lines 40-60). The methods comprise the step of: (a) detecting reporter gene product Signals from each of a

plurality of different, separately isolated cells of a target organism, wherein each of said cells contains a recombinant construct comprising a reporter gene operatively linked to a different endogenous transcriptional regulatory element (e.g. promoter) of said target organism such that said transcriptional regulatory element regulates the expression of said reporter gene, wherein said plurality of cells comprises an ensemble of the transcriptional regulatory elements of said organism sufficient to model the transcriptional responsiveness of said organism to a drug; (b) contacting each said cell with a candidate drug; (c) detecting reporter gene product signals from each of said cells; (d) comparing said reporter gene product signals from each of said cells before and after contacting each of said cells with said candidate drug to obtain a drug response profile; wherein said drug response profile provides an estimate of the physiological specificity or biological interactions of said candidate drug (see e.g. Abstract; col. 1, lines 40-60; col. 6, line 51 to col. 8, line 27). The cells include yeast cells (see e.g. col. 2, lines 19-45).

It would have been obvious to a person of ordinary skill in the art at the time the invention was made to include yeast cell in a cell-based assay for screening compounds for a characteristic of interest such as physiological or biological activity as taught by Ashby et al. in the method of Still et al. One of ordinary skill in the art would have been motivated to include yeast cell in a cell-based assay for screening compounds for a characteristic of interest such as physiological or biological activity in the method of Still et al. for the advantage of model system to obtain preliminary information on compound specificity in higher eukaryotes, such as human (Ashby: col. 2, lines 19-26). Additionally, both Still et al. and Ashby et al. disclose gene product signal expressed by the cells (Still: col. 30, lines 35-36; Ashby: col. 1, lines 42-43). Furthermore, one of ordinary skill in the art would have reasonably expectation of success in the

combination of Still et al. and Ashby et al. because Ashby et al. disclose by example the method of determining the compound characteristic of interest such as physiological or biological activity using yeast cells (Ashby: col. 10, line 34 to col. 11, line 60).

26. Claims 2-7, 9-10, 18-20, 30-31, and 33 are rejected under 35 U.S.C. 103(a) as being unpatentable over Still et al. (US Patent 5,565,324) and Misko et al. (*Analytical Biochemistry*, **1993**, 214(1):11-16).

The instant claim 2 recites a method of identifying a test compound that affects a biological event of interest. The method comprises the steps of: 1) providing a plurality of test compounds; 2) providing cells containing an inducible reporter gene, wherein expression of the reporter gene results in the production of a reporter gene product; 3) contacting the cells with the plurality of test compounds; and 4) identifying test compounds which promote or inhibit a biological event based on production of the reporter gene product. The reporter gene product is secreted by the cell, detectable, and its the presence indicates occurrence or non-occurrence of a selected biological event.

Still et al. teach methods and composition for encoding combinatorial chemistry (see e.g. Abstract; col. 3, lines 6-45). The methods includes the combinatorial synthesis that employs definable beads upon, which reactions are performed and to which the identifiers are bound, the method of screening the beads carrying the final product compounds for a characteristic of interest, and the method of analyzing the identifier tags attached to the solid supports for the reaction history of the final product compounds (see e.g. col. 3, lines 39-45; col. 5, lines 34-64; col. 29, line 65 to col. 30, line 51; col. 32, lines 14-22). The screening method comprises the steps of: 1) providing a plurality beads carrying the final product compounds (refers to claim 10 and step 1) (see e.g. col. 30, lines 1-6); 2) providing cells wherein binding a surface membrane

protein (refers to reporter gene) produces an observable product (refers to reporter gene product) that is expressed (refers to claim 18 and step 2) (see e.g. col. 30, lines 32-42); 3) the final product compounds is detach from the bead in order to react with the cells (refers to step 3) (see e.g. col. 30, lines 13-15); 4) identifying the final product compounds that cause the expression of the observable product (refers to step 4) (see e.g. col. 30, lines 42-44; col. 32, lines 14-22). The final product compounds is attached to the bead via a cleavable linker that can be cleave by irradiation with light (refers to claims 3-4) (see e.g. col. 13, lines 44-64). Furthermore, the identifier tag attached to the solid supports is analyzed for the reaction history of the final product compounds (refers to claim 33) (see e.g. col. 6, lines 18-55; col. 26, lines 57-62; col. 32, lines 14-22).

The method of Still et al. does not expressly include using a nitric oxide molecular sensor for detecting NO synthase activity in a cell based assay that screens compounds for a characteristic of interest such as physiological or biological activity and the nitric oxide molecular sensor is 2,3-diaminonapthalene (DAN).

Misko et al. disclose a cell based assay for monitoring NA synthase activity using 2,3-diaminonapthalene (DAN) (see e.g. Abstract; pg. 12, left col., line 6-28; pg. 12, right col., line 32-39; pg. 13, left col., line 25 to right col., line 10; pg. 15, right col., line 12 to pg. 16, left col., line 17). This method provides a simple yet sensitive fluorometric determination of NO synthase activity in a 96-well plate format (pg. 11, right col., lines 27-35).

It would have been obvious to a person of ordinary skill in the art at the time the invention was made to include the use of a nitric oxide molecular sensor for detecting NO synthase activity in a cell based assay that screens compounds for a characteristic of interest such as physiological or biological activity and the nitric oxide molecular sensor is 2,3-

diaminonapthalene (DAN) as taught by Misko et al. in the method of Still et al. One of ordinary skill in the art would have been motivated to include the use of a nitric oxide molecular sensor for detecting NO synthase activity in a cell based assay that screens compounds for a characteristic of interest such as physiological or biological activity and the nitric oxide molecular sensor is 2,3-diaminonapthalene (DAN) in the method of Still et al. for the advantage of providing a simple yet sensitive fluorometric determination of NO synthase activity in a 96-well plate format (Misko: pg. 11, right col., lines 27-35). Furthermore, one of ordinary skill in the art would have reasonably expectation of success in the combination of Still et al. and Misko et al. because Misko et al. shown the success of using 2,3-diaminonapthalene (DAN) for detecting NO synthase activity in a cell based assay (Misko: pg. 13, left col., line 25 to pg. 14, right col., line 50).

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to MY-CHAU T TRAN whose telephone number is 571-272-0810. The examiner can normally be reached on Mon.: 8:00-2:30; Tues.-Thurs.: 7:30-5:00; Fri.: 8:00-3:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, ANDREW WANG can be reached on 571-272-0811. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

mct
September 9, 2004

PADMASHRI PONNALURI
PRIMARY EXAMINER